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The impact of long-term moderate and heavy alcohol consumption on incident atherosclerosis among persons living with HIV

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Abstract

Background—Level of alcohol consumption is associated with differential risk of atherosclerosis, but little research has investigated this association among HIV+ persons. We evaluated the association between long-term alcohol use and incident atherosclerosis among HIV+ persons.

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Contributors

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XC – Study concept and design, interpretation, critical review of manuscript.
SS – Interpretation, critical review of manuscript.
RK – Study co-ordination, participant recruitment, data collection, interpretation, critical review of manuscript.
WP – Study co-ordination, participant recruitment, data collection, interpretation, critical review of manuscript.
RC – Study concept, design, interpretation, critical review of manuscript
All authors have approved the final article version.

Conflict of interest

The authors report no conflicts of interest.

Methods—We utilized data from HIV+ participants of the Women's Interagency HIV Study (n = 483) and the Multicenter AIDS Cohort Study (n = 305) without history of cardiovascular disease. Atherosclerosis was assessed two times by B-mode carotid artery ultrasound imaging from 2004 to 2013. Presence of plaque was defined as focal carotid intima-media thickness over 1.5 mm. Those with no plaque at baseline and plaque at follow-up were considered incident cases of atherosclerosis. Group-based trajectory models were used to categorize participants into 10-year drinking patterns representing heavy, moderate, or abstinent-low. Multivariable logistic regressions were conducted to assess the association of long-term moderate and heavy use on atherosclerosis, compared to abstinent-low.

Results—Heavy alcohol consumption was not statistically significantly associated with risk for incident atherosclerosis in women (AOR 1.10, CI 0.40–3.02) or men (AOR 1.31, CI 0.43–4.00), compared to abstinence-low. Moderate consumption was associated with 54% lower odds for incident disease in men (AOR 0.46, CI 0.21–1.00), but not in women (AOR 1.08, CI 0.58–2.00). In cohort-combined analyses, alcohol consumption was not statistically significantly association with incident atherosclerosis (moderate AOR 0.78, CI 0.48–1.27; heavy AOR 1.33, CI 0.66–2.69).

Conclusion—Moderate alcohol consumption was associated with a significant protective effect on incident atherosclerosis in men only. No other levels of alcohol consumption significantly predicted atherosclerosis in men and women compared to abstinent-low.

Keywords

HIV; Cardiovascular disease; Atherosclerosis; Subclinical; Carotid artery; Alcohol; Longitudinal

1. Introduction

There is little research investigating the association between alcohol consumption and subclinical cardiovascular disease (CVD), also known as atherosclerosis, among persons living with HIV (PLWH). Atherosclerosis is characterized by arterial plaques that may narrow the lumen, decrease blood flow and consequently predispose individuals to acute thrombotic events (National Institute of Health, 2011). In the general population, light and moderate alcohol use have been cross-sectionally associated with lower risk for carotid artery plaque (Kohsaka et al., 2011) and stiffness (Hougaku et al., 2005), compared to abstinence. Heavy alcohol use, however, has been shown to significantly increase carotid intima medial thickness (cIMT; Zyriax et al., 2010) and stiffness (Hougaku et al., 2005), consistent with a J-curved association found in the literature (Xie et al., 2012; Mukamal et al., 2003a). Similarly, a longitudinal study of 20-year drinking patterns found that consistent heavy use was associated with a significant increase in cIMT, compared to consistent moderate use (Britton et al., 2016). Other studies have found no significant association between alcohol consumption and cIMT or presence of carotid plaques (Zureik et al., 2004; Bauer et al., 2013). Further, some studies have found significant associations between alcohol consumption and subclinical disease in men, but not in women (Schminke et al., 2005; Zyriax et al., 2010; Lee et al., 2009).

The mechanism by which alcohol consumption is thought to effect cardiovascular health is not well understood, and is of great practical importance given the widespread and global

consumption of alcohol (Freiberg and So-Armah, 2016). Biological and behavioral mechanisms have been proposed to account for the higher burden of CVD among PLWH. First, heavy alcohol consumption and CVD are affected by demographic and psychosocial factors, including age, race/ethnicity, and socioeconomic status (Galvan et al., 2002; Conen et al., 2009). Second, alcohol use is significantly associated with traditional CVD risk factors, including insulin resistance (type II diabetes; Míguez-Burbano et al., 2009), tobacco use (Cook et al., 2013), and illicit drug use (Conen et al., 2009; Cook et al., 2013; Chitsaz et al., 2013). Third, HIV-infection alone increases systemic inflammation (Shrestha et al., 2014; Bahrami et al., 2016) and immune activation (Maniar et al., 2013; Strategies for Management of Antiretroviral Therapy (SMART) Study Group et al., 2006; Hsue et al., 2009; Neuhaus et al., 2010), which are pathophysiologic responses that contribute to the risk for CVD (Bahrami et al., 2016; Hsu et al., 2016; Hansson, 2005). Chronic inflammation and immune activation can lead to the breakdown of the endothelial walls of the gastrointestinal tract, a process that leads to microbial translocation, which triggers further immune and pro-inflammatory responses (Maniar et al., 2013; D'Abramo et al., 2014; Klatt et al., 2013). While low level consumption of alcohol may have favorable lipid or antithrombotic effects, low levels of alcohol use have been shown to increase systemic inflammation, as well as risk for microbial translocation (Brenchley and Douek, 2012).

A recent systematic review found the current state of the literature to be limited to mostly cross-sectional studies and/or investigation of imprecise measures of alcohol use (e.g., any alcohol use, alcohol abuse/dependence history) to characterize risk among majority male HIV infected persons (Kelso et al., 2015). While these studies help us begin to understand the importance of alcohol consumption on cardiovascular health, study participants were majority male (78–100%) and most studies utilize only medical records to classify diagnosis of clinical CVD, and do not assess early stages of disease development, such as atherosclerosis.

The objective of the current analysis was to assess the association between 10-year patterns of alcohol use and the incidence of subclinical atherosclerosis, measured by B-mode carotid artery ultrasound imaging. Specifically, we aimed to 1) test the association between long-term moderate and heavy alcohol use and subclinical atherosclerosis among PLWH, and 2) to explore whether the relationships appeared to differ by gender. We hypothesized that long-term moderate and heavy alcohol use would be significantly associated with increased risk for incident subclinical atherosclerosis.

2. Material and methods

2.1. Study setting, selection, and inclusion criteria

The Multicenter AIDS Cohort Study (MACS; Kaslow et al., 1987; Detels et al., 1992; Dudley et al., 1995) and Women's Interagency HIV Study (WIHS; Barkan et al., 1998; Bacon et al., 2005) are well-established, national multicenter cohorts of men who have sex with men (MSM) and of women, respectively, living with or at risk for HIV-infection. Participants from MACS were recruited from the following metropolitan areas: Baltimore, MD, Washington, DC, Chicago, IL, Pittsburgh, PA, Los Angeles, CA. Participants from WIHS were recruited from the following metropolitan areas: Brooklyn and Bronx, NY,

Washington, DC, Chicago, IL, Los Angeles and San Francisco, CA. The MACS recruited MSM across three waves, in 1984–1985 (n = 4954), 1987–1991 (n = 668), and 2001–2003 (n = 1350). Women were recruited in WIHS across two waves, in 1994–1995 (n = 2625) and 2001–2002 (n = 1141). Data were collected through structured interviews, and standardized physical, psychological, and laboratory assessments. HIV status was assessed by enzyme-linked immunosorbent assay (ELISA) with Western blot for confirmation at study enrollment for HIV+ participants, and semi-annually for HIV- participants. Written informed consent was obtained prior to each semi-annual assessment for both cohorts. The questionnaires are available online for MACS at http://aidscohortstudy.org and for WIHS at https://statepi.jhsph.edu/wihs/wordpress/.

The WIHS cardiovascular sub-study recruited women aged 25–60 years, with no history of CVD (n = 1321); The MACS cardiovascular sub-study recruited men over 40 years of age, under 300lbs, and with no history of CVD (n = 828). The current study focused on those with sero-prevalent HIV at baseline and excluded those with less than four alcohol use assessments prior to the first atherosclerosis assessment (WIHS: n = 118; MACS: n = 216). We chose four alcohol consumption measurements as an exclusion criteria because we wanted to be able to detect different types of change. Less than four measurements would not allow accurate modeling of quadratic or cubic change, if present. Further, those in the 10-year abstinent-low and moderate consumption patterns, who reported past heavy drinking at enrollment were excluded from the analysis (MACS: n = 4 from the abstinent-low, n = 15 from moderate; WIHS n = 10 from the abstinent-low, n = 19 from the moderate). Those who screened positive for atherosclerotic lesions at baseline or those who did not have two carotid ultrasound assessments were not included in the assessment of incident atherosclerosis. The final sample sizes were n = 483 in WIHS and n = 305 in MACS. The median person-years of follow-up from 1994 to 2014 was 16.7 years (interquartile range [IQR]: 16.0-18.5 years) for WIHS participants and 12.4 years (IQR: 10.0-16.5 years) for MACS participants. This analysis was approved by the Institutional Review Board at the University of Florida.

2.2. Data collection

In addition to the standard data collection for the MACS and WIHS, participants in the cardiovascular sub-studies underwent high-resolution B-mode carotid artery ultrasounds of six locations in the right carotid artery (the near and far walls of the common carotid artery [CCA], carotid bifurcation, and internal carotid artery [ICA]; Hodis et al., 2001), using a standardized protocol across study sites (Kaplan et al., 2008). Quality control and reliability of the carotid artery ultrasound measurement was performed among a subset of WIHS and MACS participants and was found to have high intraclass correlations (ICC) in both WIHS (variation coefficient = 1.8%; ICC = 0.98) and MACS (variation coefficient = 1.0%; ICC = 0.99; Kaplan et al., 2008).

2.2.1. Main outcome measure—Subclinical atherosclerosis was defined as the presence of an arterial lesion or plaque, which was a focal cIMT greater than 1.5 mm (Stein et al., 2008) and was measured up to two times from 2004 to 2013. The first measurement occurred between 2004 and 2006 and the second between 2011 and 2013 for both MACS

and WIHS. Participants who screened negative for lesions or plaques at the baseline assessment, but positive at follow-up were considered incident cases. Therefore, those who were positive for lesions at baseline or those who did not have two carotid ultrasound assessments were not included in the assessment of incident atherosclerosis.

2.2.2. Independent variable—Participants self-reported the average frequency (number of days per week) and quantity (number of drinks per drinking day) of alcohol use. The average number of drinks per week was calculated by multiplying the frequency by the quantity. For optimal model convergence, the number of drinks per week were capped at 14 for women and 21 for men in accordance with the definition of hazardous alcohol use (Reid et al., 1999).

2.2.3. Covariates—All covariates were chosen based on previous literature and were measured at the time of incident atherosclerosis assessment. Age was assessed in years, using participants' self-reported date of birth. Self-reported race was categorized as white, black, and Asian/Pacific Islander or Native American/Alaskan. Self-reported smoking was assessed in number of packs smoked using standardized categories: less than half a pack per day; at least half a pack but less than one pack per day; at least one but less than two packs per day; two or more packs per day. Cumulative pack-years were calculated to determine the average pack, multiplied by 0.5 to reflect the semi-annual visits, and summed across the years just prior to the carotid artery ultrasound assessments. Self-reported illicit drug use included any of the following: cocaine; amphetamine-type stimulants; heroin or other opiates and was dichotomized. Plasma HIV RNA viral load was measured using standard laboratory techniques and was categorized as < 200 copies/mL or ≥200 copies/mL. Hepatitis C Co-infection (HCV) was measured via HCV viral RNA and antibody and was dichotomized as having ever had HCV RNA positively or not. CD4+ T-cell count was assessed for collinearity with HIV RNA viral load; because of collinearity and poorer fitting models with both HIV viral load and CD4+ T-cell count in the model, as well as with CD4+ T-cell count only in the model, CD4+ T-cell count was not included as a covariate. Cardiovascular-related factors that mediate the relationship between alcohol consumption and atherosclerosis were not included as confounding factors (i.e., cholesterol, blood pressure, and triglyceride, body mass index, diabetes) (Vu et al., 2016; Brinton, 2012).

2.3. Data analyses

2.3.1. Group-Based trajectory models—To describe patterns of alcohol consumption over time, we conducted group-based trajectory models (GBTM). Group-based trajectory models were used to categorize participants into 10-year drinking patterns representing heavy, moderate, or abstinent/low. In the first modeling step, we assessed linear patterns of 3–5 groups, as suggested by previous research (Cook et al., 2013; Marshall et al., 2015a; Marshall et al., 2015b). Goodness-of-fit was assessed at each step using the Akaike information criteria and Bayesian information criteria (smaller the values, better the model), group posterior probabilities (PP ≥ 0.7 is indicative of sufficient internal reliability), and mean model entropy (≥ 0.7 is optimal; summed PP/number of groups). The PP estimate is the probability that any one group-based trajectory adequately captures the individual patterns. Therefore, an individual pattern was assigned into the group pattern with the

highest probability of group membership. Models with PP and/or model entropy values < 0.7 were rejected (Andruff et al., 2009). The 95% confidence intervals (CI) of the resulting patterns were used to qualitatively assess the stability of the trajectories. Models with small CIs of trajectories were favored over wide CIs. Separately, for each cohort, group-based trajectory modeling was conducted to describe 10-year drinking patterns prior to the incidence of atherosclerosis. Trajectories that described weekly drinking of 1–7 drinks for women and 1–14 drinks for men were labeled as "Moderate", and those that described consistent weekly drinking of > 7 drinks for women and > 14 drinks for men were labeled as "Heavy".

2.3.2. Multivariable logistic regression models—Crude and adjusted associations between alcohol consumption patterns and the incidence of subclinical atherosclerosis were conducted using separate logistic regression models, first stratified by gender and then with cohorts combined. Multivariable adjustment of the aforementioned covariates was conducted in all logistic regression models in a stepwise fashion, with demographic factors (i.e., age, race/ethnicity, gender when applicable) being added first, followed by substance use (i.e., pack years, illicit drug use), and HIV-related factors (i.e., RNA viral load, HCV). Compared to the lowest alcohol consumption pattern, other alcohol consumption patterns were considered statistically significantly associated with incident subclinical atherosclerosis at the p-value < 0.05 level. All statistical analyses were conducted using SAS 9.4 (SAS Institute, Inc., Cary, NC).

3. Results

Sample characteristics by cohort at the time of incident atherosclerosis measurement are presented in Table 1. There were 483 HIV+ women and 305 HIV+ men who met study criteria at follow-up. Mean age (years) was about 51 in women and 65 in men. Women were more likely to be of black race than men (63% vs. 44%, $p < 0.001$). Men were more likely to report illicit drugs use (16% vs. 7%, $p < 0.001$) and women had higher mean smoking pack-years (women 2.6 [IQR 0.0–3.8]; men 1.7 [0.0–2.1]). Hepatitis C co-infection (women 14%; men 16%, p=0.37) was similar by gender. Men were more likely to have suppressed viral load (90% vs. 72%, $p < 0.001$) compared to women.

3.1. 10-year alcohol consumption trajectories

A three-group trajectory model emerged as the best fitting model for women (Fig. 1, Panel A; model entropy 0.98) and men (Fig. 1, Panel B; model entropy 0.98). Alcohol consumption patterns included "Abstinent/low" (WIHS 47%; MACS 19%, very little to no consumption throughout 10-years), "Moderate" (WIHS 43%; MACS 72%, moderate consumption throughout 10-years) and "Heavy" (WIHS 10%; MACS 9%, heavy consumption throughout 10-years).

3.2. Incident subclinical atherosclerosis

Incident subclinical atherosclerosis was detected in 12% of women (n = 57) and 17% of men (n = 52). Crude and adjusted odds ratios of alcohol consumption patterns on incident subclinical atherosclerosis are presented in Table 2. Long-term heavy alcohol use was not

statistically significantly associated with increased risk for incident sub-clinical atherosclerosis in women (AOR 1.10, CI 0.40-3.02, p=0.85) and men (AOR 1.31, CI 0.43-4.00, p=0.63). While moderate alcohol use was significantly associated with a protective effect on incident subclinical atherosclerosis in men (AOR 0.46, CI 0.21-1.00, p=0.05), a similar trend was not found in women (AOR 1.08, CI 0.58-2.00, p=0.81), after controlling for race, age, pack-years, illicit drug use, hepatitis c co-infection, and suppressed viral load. In the analysis that combined both cohorts, heavy (AOR 1.33, CI 0.66-2.69, p=0.42) and moderate (AOR 0.78, CI 0.48-1.27, p=0.32) alcohol consumption were not statistically significantly associated with incident subclinical atherosclerosis, compared to abstinent-low use. Full model estimates are available in Supplemental Table 1 (by cohort) and Supplemental Table 2 (cohort-combined). In exploratory analyses (data not shown), moderate consumption, compared to heavy consumption was associated with significantly lower odds for incident atherosclerosis in men (AOR 0.35, 95% CI 0.13-0.92, p=0.03), but not in women (AOR 0.98, 95% CI 0.35-2.70, p=0.96).

4. Discussion

The aim of this analysis was to assess the association between 10-year patterns of alcohol use and the incidence of atherosclerosis, measured by B-mode carotid artery ultrasound. Specifically, we tested the general assumption that moderate alcohol consumption is protective for cardiovascular health among PLWH. Contrary to our hypothesis, long-term heavy alcohol use was not statistically significantly associated with incident atherosclerosis. These results are contrary to previous studies that have demonstrated an association between heavy alcohol use and subclinical atherosclerosis in the general population (Zyriax et al., 2010; Hougaku et al., 2005; Xie et al., 2012; Mukamal et al., 2003a,b) and related literature finding positive associations between heavy alcohol use and clinical cardiovascular disease among PLWH (Justice et al., 2008; Corral et al., 2009; Freiberg et al., 2010). However, this finding is consistent with recent studies showing no association between heavy drinking and cardiovascular disease among PLWH (Wandeler et al., 2016; Kelly et al., 2016; Womack et al., 2014) and subclinical atherosclerosis in the general population (Zureik et al., 2004; Bauer et al., 2013; Kim et al., 2014). It is possible that heavy alcohol use is a contributor to risk for clinical cardiovascular disease, but less predictive at the developmental stages of atherosclerosis. An additional explanation could be that abstinent-low drinkers had a history of heavy drinking that is not captured in either drinking at enrollment or the 10-year patterns. If past heavy drinking prior to enrollment conferred increased risk, then the effect of current 10-year patterns of heavy drinking could be attenuated when compared to the current abstinent-low drinkers.

We found that long-term moderate alcohol use was statistically significantly associated with a reduction in odds for incident atherosclerosis in men. This finding is consistent with other research indicating a protective effect between moderate alcohol consumption and subclinical atherosclerosis in the general population (Kohsaka et al., 2011; Hougaku et al., 2005), as well as in extent research on clinical disease in the general population (McElduff and Dobson, 1997; Sacco et al., 1999; Corrao et al., 2000; Mukamal et al., 2003b; Reynolds et al., 2003) and among PLWH (Wandeler et al., 2016; Carrieri et al., 2012; Schminke et al., 2005). Other studies have found inconsistent alcohol effects on subclinical atherosclerosis

between women and men (Schminke et al., 2005; Zyriax et al., 2010; Lee et al., 2009). Gender differences may be a result of the differences in risk factors and the clinical presentation of CVD. For example, subclinical disease in women is more likely to present as microvascular coronary disease, rather than plaque development and narrowing of the large coronary arteries (Vaccarino and Bremner, 2016). Therefore, it is possible that moderate and heavy drinking are associated with early progression of CVD, but in the small arteries and vessels of the coronary arteries. Finally, it is important to note that, given the p-value and the secondary nature of the current analyses, there may be no real association between moderate drinking and atherosclerosis in men living with HIV. More research that is powered to investigate the specific effects of different long-term and short-term drinking patterns is needed to further understand the possible J-curved relationship between alcohol consumption and atherosclerosis among PLWH.

4.1. Limitations

The readers should consider some limitations of the current study. First, frequency and quantity of alcohol consumption were assessed via self-report and are subject to recall and social desirability biases, resulting in potentially inaccurate reports of alcohol consumption. However, this method has been established as a reliable and valid approach to alcohol use assessment (Del Boca and Darkes, 2003). Second, while we did exclude those in the 10-year abstinent-low and moderate consumption patterns who reported heavy drinking at enrollment, we could not account for drinking prior to cohort enrollment. Therefore, it is impossible to know if participants were ever heavy drinkers or ever had an alcohol use disorder. Third, because we used carotid artery ultrasound, these results can only be generalized to disease within the carotid artery and may not extend to plaque or lesions outside of this area. Carotid artery ultrasound also does not capture all mechanisms that are involved in atherothrombotic events, being most strongly associated with blood pressure levels (Sander et al., 2000) and bearing little relationship with coagulation (Sosef et al., 1994) or platelet activity (De Luca et al., 2010), for example. However, research has found presence of plaque or lesions within the carotid artery to be highly correlated to subclinical disease in other vascular territories when compared to other methods that detect low to no disease (Lester et al., 2009; Davis et al., 1999). While we did not aim to investigate clinical CVD, subclinical atherosclerosis is a proximal indicator of later clinical manifestations of CVD, such as myocardial infarction and stroke. Fourth, there are significant demographic differences between the WIHS and MACS cohorts, making direct comparisons of stratified analyses difficult. Because of these differences, we carefully controlled for variables related to demographics and behavioral risk. Fifth, GBTM is a semi-parametric and probabilistic model that estimates grouped trajectories of the most similar individual patterns. Therefore, each trajectory group does not fully describe the individual-level patterns contained within them and should not be considered absolute. Further, we restricted our analyses to participants with at least four alcohol consumption assessments in order to estimate trajectory models. Therefore, it is possible that different trajectories could have emerged had we not excluded these participants.

5. Conclusions

In summary, the current study adds to the literature on the effect of longitudinal alcohol consumption on CVD among PLWH, by focusing on early subclinical manifestations of CVD. This study provides important new information regarding the specific effect of moderate alcohol use, and thus helps fill the gap in this area of alcohol research. Future research should continue to investigate the effect of alcohol use on atherosclerosis and interactions with other significant factors, such as mental health issues, social support, and antiretroviral treatments. It is possible, that through this continued research, we may be able to identify subgroups of drinkers that are at greater risk for CVD, by which tailored interventions can target. Further, validation of the J-curve association could focus on the proposed risk mechanisms between alcohol consumption and cardiovascular health. For example, if moderate consumption is protective, we would expect a decrease in proinflammatory (i.e., C-reactive protein, interleukin-6, tumor necrosis factor) and cardiac biomarkers (i.e., creatine kinase, myoglobin, cardiac troponins).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.drugalcdep.2017.09.034.

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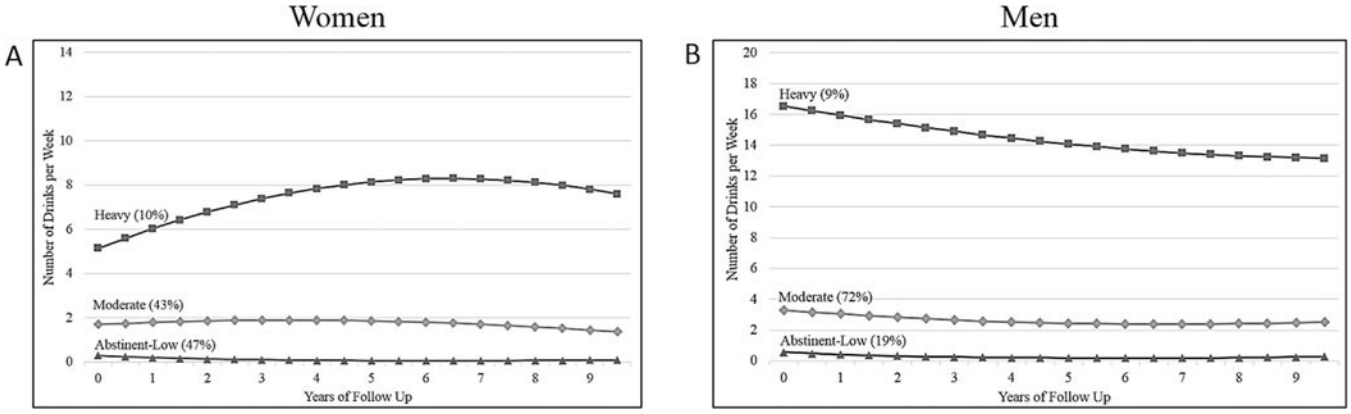

Fig. 1.

10-year alcohol consumption trajectories by cohort.

Panel A: Alcohol consumption patterns in women prior to incident atherosclerosis assessment; Panel B: Alcohol consumption patterns in men prior to incident atherosclerosis assessment

Table 1

Sample characteristics of women and men living with HIV by cohort.

Characteristics	Women (N = 483)	Men (N = 305)	P
Race			< 0.001
White	96 (20)	127 (42)	
Black	307 (63)	133 (44)	
Other (Asian, Native American, etc.)	80 (17)	45 (15)	
Age, mean (IQR)	50.6 (45.5–54.8)	65.3 (60.7–70.5)	< 0.001
Smoking pack-years, mean (IQR)	2.6 (0.0–3.8)	1.7 (0.0–2.1)	< 0.01
Illicit drug use			< 0.001
No	451 (93)	257 (84)	
Yes	32 (7)	48 (16)	
Hepatitis C status			0.37
Negative	415 (86)	255 (84)	
Positive	68 (14)	50 (16)	
HIV RNA Viral Load			< 0.001
< 200 copies/mL	346 (72)	273 (90)	
≥ 200 copies/mL	137 (28)	32 (10)	
10-year alcohol consumption pattern			< 0.001
Abstinent-Low	226 (47)	59 (19)	
Moderate	210 (43)	218 (72)	
Heavy	47 (10)	28 (9)	
Incident lesions			0.04
No	426 (88)	253 (83)	
Yes	57 (12)	52 (17)	

Abbreviations: IQR, interquartile range

Table 2

Association between 10-year alcohol consumption patterns and incident subclinical atherosclerosis, overall and by cohort.

	Women's Interagency HIV Study				Multicenter AIDS Cohort Study				Combined			
	Crude OR (95% CI)	***P***	**Adjusted OR[a] (95% CI)**	***P***	**Crude OR (95% CI)**	***P***	**Adjusted OR[a] (95% CI)**	***P***	**Crude OR (95% CI)**	***P***	**Adjusted OR[a] (95% CI)**	***P***
Alcohol Consumption Patterns												
Abstinent-Low	Reference				Reference				Reference			
Moderate	0.91 (0.50–1.64)	0.74	1.08 (0.58–2.00)	0.81	0.51 (0.25–1.05)	0.07	0.46 (0.21–1.00)	0.05	0.84 (0.54–1.30)	0.44	0.78 (0.48–1.27)	0.32
Heavy	1.29 (0.53–3.17)	0.58	1.10 (0.40–3.02)	0.85	1.29 (0.47–3.55)	0.63	1.31 (0.43–4.00)	0.63	1.49 (0.77–2.86)	0.23	1.33 (0.66–2.69)	0.42

OR, Odds Ratio.

[a]Controlled for race, age, illicit drug use, pack years of cigarette use, Hepatitis C co-infection, and suppressed viral load.